Asymptomatic Severe Mitral Valve Regurgitation
Observation or Operation?

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Management of patients with mitral valve regurgitation (MR) has changed dramatically over the past 20 years; this change is largely attributable to 3 factors. First, there have been significant improvements in operative techniques that have led to predictable and durable results after valve repair. In current practice at our clinic, >95% of patients with pure MR caused by degenerative diseases have valve repair rather than prosthetic replacement, and with modern, simplified methods of leaflet repair and annuloplasty, the risk of reoperation after correction of MR is no greater than that after mitral valve replacement.1

The second major shift in mitral valve disease is the change in pathology and pathophysiology of MR. In current practice, almost 80% of patients having mitral valve operations have pure regurgitation rather than valve stenosis or mixed regurgitation and stenosis, and the cause is most often degenerative or myxomatous disease; there is a declining frequency of postinflammatory disease in North America and many other areas of the world.

The third important change in the management of patients with mitral valve disease is the better understanding of the natural history of MR, which has been made possible by both detailed natural history studies and improved techniques of 2-dimensional and Doppler echocardiography.2–4 The article by Kang et al5 in this issue of Circulation provides important new and confirmatory information on the outcome of asymptomatic patients with severe MR.

Before the 1990s, most clinicians viewed MR as a relatively benign condition, and surgery was reserved for patients who were severely symptomatic or failed medical management.6,7 Reluctance to proceed with operation was related to the likelihood of prosthetic valve replacement and to the notion that asymptomatic patients with severe MR were a stable compensated group with negligible risk of serious complications, including sudden death.

In 1996, Ling and colleagues8 reported the late outcome of 229 patients with flail mitral valve leaflets, an echocardiographic finding that is almost uniformly associated with severe valve leakage. In that observational study, 45 patients (20%) died under medical management; 31 of the 45 deaths (69%) were due to cardiac causes. Actuarial survival of patients with MR was significantly less than an age- and gender-matched cohort even though corrective surgery was not withheld. Rather, clinicians managed patients according to standard practice, which, in most instances, involved correction of MR after observation/medical treatment had failed. The presence of severe symptoms at the time of diagnosis of MR was a major predictor of subsequent death, but annual mortality was 4.1% in patients who were in New York Heart Association class I or II, and more than a third of all cardiac-related deaths occurred in patients who did not have preceding class III or IV symptoms. Importantly, multivariate analysis suggested that surgery performed at any time was an independent predictor of improved survival.

A further analysis of 221 patients with flail mitral valve leaflets stratified patients according to the timing of surgery.9 Patients who underwent mitral valve surgery within 1 month of diagnosis had improved overall survival compared with those managed conservatively (10-year survival, 79% versus 65%; P=0.028). The beneficial effect of early surgery was observed in asymptomatic and minimally symptomatic patients and in those with clinical heart failure. An analysis of the causes of death also strongly indicated that the beneficial effect of MR correction was due to improved postoperative cardiovascular physiology and not simply patient selection.

Recent data also suggest that even asymptomatic patients with severe MR are at increased risk for cardiac complications. Enriquez-Sarano et al10 studied outcome of 456 prospectively enrolled patients who had quantitative assessment of MR (mean regurgitant volume, 66±40 mL per beat; mean effective regurgitant orifice area, 40±27 mm²). Among these asymptomatic patients with severe MR, the estimated 5-year risk of death was 22%, and the risk of any cardiac event (death resulting from cardiac causes, heart failure, or new atrial fibrillation) was 33%. Patients with an effective regurgitant orifice area of at least 40 mm² had a 5-year survival rate that was lower than that expected on the basis of US Census data (58±9% versus 78%; P=0.03). On multivariate analysis, those patients with an orifice of at least 40 mm² had an increased risk of death resulting from any cause (adjusted risk ratio, 2.90; P<0.01), death resulting from cardiac causes (adjusted risk ratio, 5.21; P<0.01), and cardiac events (adjusted risk ratio, 5.66; P<0.01). Cardiac surgery was performed in 232 patients during an average follow-up of 5 years, and correction of MR was independently associated with improved survival (adjusted risk ratio, 0.28; P<0.01). Some clinicians have been reluctant to apply the findings of these investigations to the management of patients with
Among patients having early surgery, valve repair was results that can be achieved with surgical correction of MR. populations. In the present study by Kang et al, average left ventricular end-diastolic dimension was 58 mm. In the investigation by Rosenhek et al, the most obvious likely reason for the in this relatively young population of patients (average age, 50 years). So, what are the possible explanations for the different outcomes reported in this study and the previous investigation by Rosenhek et al? The most obvious likely difference is the severity of valve leakage in the 2 patient populations. In the present study by Kang et al, average effective regurgitant orifice area was >0.88 cm², and average left ventricular end-diastolic dimension was 58 mm. In the study from Vienna, MR was graded in a semiquantitative manner, and the average left ventricular end-diastolic dimension was 56 mm. These differences in degree of ventricular enlargement are likely greater if one takes into account differences in body size between the European and Asian populations.

Results of the present study also confirm the very good results that can be achieved with surgical correction of MR. Among patients having early surgery, valve repair was accomplished in 94%, and there were no early deaths during valve repair or replacement. Only 2 of the 151 patients having early surgery required reoperation during follow-up.

The unstated risk in managing asymptomatic patients conservatively (“watchful waiting”) is that some will be lost to follow-up, and other patients will not return to medical attention until symptoms or complications develop. Indeed, even in this controlled, prospective study with annual examinations and echocardiograms, 6 patients died of congestive heart failure, 4 patients died suddenly (3 were asymptomatic), and 2 died of endocarditis. Unfortunately, operative risk increases and there is excess long-term postoperative mortality and morbidity in patients with severe MR and New York Heart Association class III or IV symptoms. This fact and the results of the study by Kang and associates should lead to the consideration of surgical correction of severe organic MR when no or minimal symptoms are present in patients at low operative risk, especially if repair is feasible.

Disclosures
None.

References

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MR who are completely asymptomatic. In an observational study of 132 patients, Rosenhek and associates concluded that mitral valve surgery can be delayed in asymptomatic patients until either symptoms occur or there is echocardiographic evidence of systolic dysfunction, progressive ventricular enlargement, or elevated pulmonary artery pressure, but the patients in this study from Vienna were almost a decade younger than those previously cited, and the degree of MR may not have been severe in all patients.

So, it is in this debate on asymptomatic patients with severe MR that the data from Kang and associates are so important. In this prospective clinical study of 447 patients, all of whom had severe MR determined by quantitative Doppler echocardiography, surgery was performed within 6 months of initial assessment (early surgery) in 161 patients. The remaining patients were treated in what the authors call the conventional manner and were referred for surgery if they developed exertional dyspnea, ventricular dysfunction (left ventricular ejection fraction <60%, left ventricular end-systolic dimension >45 mm), Doppler-estimated pulmonary artery pressure >50 mm Hg, or atrial fibrillation. During the median follow-up of 5 years, there were no cardiac deaths among patients who had early surgery, and 2 patients had reoperation. Among patients treated in the conventional manner, there were 12 cardiac deaths, 1 reoperation, and 22 admissions to the hospital for treatment of congestive heart failure. To control for possible bias whereby healthier patients were offered operation early, the authors adjusted for differences in baseline characteristics using propensity score, and for the 127 matched pairs, actuarial 7-year event-free survival was significantly higher in the early surgery group compared with patients treated in the conventional manner (99% versus 85%; P=0.007).

The demonstration that early intervention to correct MR improves long-term clinical outcome compared with conservative (observational) strategy supports earlier reports by Ling et al and Enriquez-Sarano and associates. Indeed, the advantage of early surgery to correct MR was apparent even in this relatively young population of patients (average age, 50 years). So, what are the possible explanations for the different outcomes reported in this study and the previous investigation by Rosenhek et al? The most obvious likely difference is the severity of valve leakage in the 2 patient populations. In the present study by Kang et al, average effective regurgitant orifice area was >0.88 cm², and average left ventricular end-diastolic dimension was 58 mm. In the study from Vienna, MR was graded in a semiquantitative manner, and the average left ventricular end-diastolic dimension was 56 mm. These differences in degree of ventricular enlargement are likely greater if one takes into account differences in body size between the European and Asian populations.

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